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A LECTURE

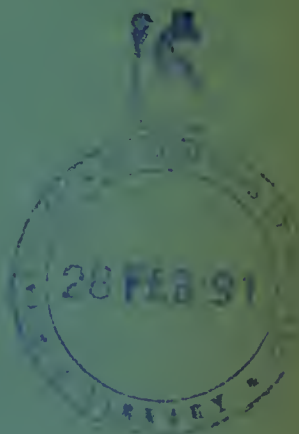
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*Delivered in the Jefferson Medical College,
January 8, 1891.*

BY

SAMUEL G. DIXON, M.D.,

BACTERIOLOGIST TO THE ACADEMY OF NATURAL SCIENCES OF PHILADELPHIA.



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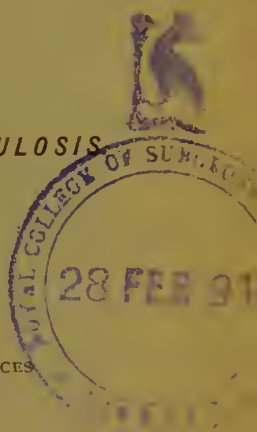
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KOCH'S METHOD OF TREATING TUBERCULOSIS

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GENTLEMEN: While in Berlin I had the opportunity of meeting many prominent men who were interested in Koch's discovery and of hearing their opinions concerning it. It may not be out of place, therefore, should I venture to state briefly my impressions regarding Koch's remedy. Here is a diagram on the right side of which you may possibly recognize stained tubercle bacilli in lung tissue, whereas on the left tubercle bacilli, double stained, are represented. When these minute single-celled micro-organisms in full vitality enter the animal economy in sufficient number to overcome the army of animal cells, whose function it is to devour all intruders, an active destruction of tissue is set up which is very difficult to overcome, unless recognized in its very incipiency. The tubercle bacillus is man's greatest enemy and tuberculosis has robbed more families of happiness than any other disease; but I am ashamed to say that there is not yet a well-endowed bacteriological laboratory in this city of nearly a million inhabitants. Studies such as those of Koch should stimulate rich men to endow laboratories for original research and teaching.

In 1889 I advanced the theory that by a thorough fil-

tering out of tubercle bacilli from tubercular matter we might obtain a fluid which could be so weakened that by systematic inoculations a change might be produced in living animal tissue that would overcome tuberculosis. The announcement of this theory was accompanied by a statement that favorable results had been obtained in animals so treated. Owing to an unavoidable delay I was unable to push my work to a close. I regret the interruption to my work, for during this time Professor Robert Koch, for whom I have the most profound respect, produced the fluid that I now hold in my hand, which probably contains less débris than any I had obtained at the time when he made his first announcement. About one one-thousandth dilution of this, it is supposed, acts upon tuberculous tissue.

The reagent is, probably, a metabolic product of the tubercle bacillus, the bacilli having been filtered out. With this active principle I am inclined to believe there are glycerin, gelatin, and some salt, probably a salt of gold. How this filtrate acts we do not know, but it may be conjectured that when the bacillus comes in contact with animal tissues it is stimulated to secrete some material which changes the chemical arrangement of the tissues and renders them capable of being absorbed.

The effect on the tissue seems to be an inflammatory one of a degree peculiar to the action of the tubercle bacillus and suited to its existence. If this be an explanation of the process, we may seek to neutralize the secretion of the bacillus and thereby prevent it from acting on the animal tissues; or again we may cultivate the organism on an artificial medium and then isolate in a concentrated form that which breaks up tuberculous tissue. This material when injected into the system which is already the habitat of the tubercle bacillus, meets with the normal secretion of that micro-organism which is present in amounts just sufficient to render the tissues suitable for the growth of the bacillus.

As soon as the artificial poison is added, the inflammatory condition of the tuberculous tissues becomes greater than that degree suited to the life of the existing micro-organisms, the tissue is killed, and with the organisms falls away from the new surface. This is but a theory, for tuberculosis is a chronic disturbance, in which the microörganism is not killed by its own product as we suppose is the case in acute infectious diseases.

Dr. T. Lauder Brunton intimates that the Koch fluid may be a product of other than the tubercle bacillus. He cites the fact that lupus has been seen to shrivel and necrose after an attack of erysipelas or measles, and that peritonitis, supposed to be tubercular, has disappeared during recovery from diphtheria.

I believe that the Koch liquid is made from or by means of the tubercle bacillus. Its action on tuberculous tissue is simply marvellous. During my short stay in Berlin I did not see the reaction take place in tissues other than those which I suspected were tuberculous, unless it was in the nodules of leprosy. The lepra tubercles seemed to change color somewhat under the action of the Koch fluid. Yet to get the characteristic reaction, a dose sufficiently large to react on a healthy person had to be administered. If it does affect leprosy tissue, it is not surprising, as the lepra bacilli that I have examined appear to be related to the tubercle bacillus. However, their smaller size and their apparent motility being the points of difference, at present I am inclined to the opinion that the reaction produced by Koch's fluid is diagnostic of tubercular tissue; yet, until its curative power is determined, we must be cautious in our use of it as a diagnostic agent, for we have been taught that inflammation which, in all probability is tuberculous, is often set up in tissue that before treatment was apparently healthy.

The common experience with lupus-cases is somewhat as follows: In about five hours after the injection of the

fluid, the temperature begins to rise, reaching its maximum quite suddenly. Then it soon falls to normal and in very anæmic patients reaches an alarmingly low degree. In one case of pernicious anæmia death soon followed the injection.

During treatment, a nodular infiltration takes place. The œdema which is present in many cases is exaggerated. As the fever subsides, prostration is often experienced, and the nodules gradually become covered with a crust under which can be detected healthy granulations. When these crusts fall off, red cicatrices are to be seen, and the surface soon presents the appearance of a perfect cure; but in some cases, after a few weeks the lupus-spots take on an inflammatory condition. We do not know how far the remedy destroys tuberculous tissue, for while it destroys recognizable tuberculous matter, the recurrence of the disease demonstrates that there may exist tuberculous tissue which the remedy will not destroy.

In the Charité Hospital I saw a case of lupus in a boy ten years old. The lesion began about the bridge of the nose and extended down on either side, involving the alæ and the skin covering both the superior and inferior maxillary regions. An injection of 0.002 gm. of Koch's fluid caused a rigor, vomiting, and a severe reaction, the temperature reaching 105° F., with the symptoms that usually follow the administration of a large dose when the area of tuberculous tissue is extensive. The patient soon became covered with a rash resembling scarlatina, and this process went on to desquamation, which involved the entire surface of the body. The lupus-tissue passed through the changes described until a healthy cicatrix was formed.

In another case of lupus, an irritating cough and harsh voice developed after the second injection. After the third injection, small clusters of red excrescences appeared on the right vocal cord. After some days

the lupus was seen to be granulating nicely, the inflammation on the vocal cord had subsided, and the cough was rapidly decreasing.

To use the liquid, a one-per-cent. solution should be prepared by placing 0.1 c.c. of the fluid into a glass vessel graduated to 10 c.c. The vessel is then filled to 10 c.c. with sterilized water. 1 c.c. of this solution contains a dose of 0.01 c.c. of the original Koch fluid. The Koch syringe that I have here is graduated in tenths up to a capacity of 1 c.c. ; therefore, if 1 c.c. of this one-per-cent. dilution be placed in the syringe, one-tenth of the syringeful will contain 0.001 c.c. of the remedy. In giving large doses, the ten-per-cent. dilution should be used.

Owing to the suppuration set up by the Koch liquid, in the vascular tissue immediately surrounding the tubercles, the remedy is positively contra-indicated in tubercular meningitis. This being so, the practitioner in treating other forms of the disease must be on the watch for indications of cerebral involvement.

Regarding its value in surgical tuberculosis, I can remember one case of resection of a rib of a patient in the Charité, in which the granulations had become indolent, and the wound absolutely refused to heal until put under the Koch treatment. Reaction was produced by the first inoculation, after which healthy granulations developed and continued up to the day that I last saw the case, which was about the tenth day after the first injection.

The therapeutic value of the fluid in joint- and bone-tuberculosis is promising. Children in the Charité Hospital suffering with hip-joint tuberculosis seemed to experience much less pain when the joints were moved after treatment with the Koch lymph. The results in cases treated with the remedy until no further reaction could be produced and then operated on by mechanically removing all the necrosed bone and tissue seemed to

be much better than those not so treated. If the necrotic parts are not removed they are likely to reinfect the system, as the débris disintegrates. This is especially so when there is a general predisposition to tuberculosis.

In one case of kidney-tuberculosis tubercle bacilli were found in the blood and urine. The remedy caused rigors and vomiting and an elevation of temperature to 105° F. When I last heard, this case was going from bad to worse.

After a successful experience with a reagent on guinea-pigs suffering from tuberculosis of the lung-tissue, I am disappointed that more has not been accomplished, but I have much faith in the ultimate triumph of the liquid over pulmonary phthisis, provided that the lesion is recognized and treated in its very incipiency. It must be borne in mind that the guinea-pigs which I have cured were in all probability not predisposed to tuberculosis. The remedy may render tissues more susceptible to the action of bacilli than before its introduction. Further, it may even disseminate bacilli into tissue that otherwise would never have become tuberculous. Should the dissemination of tuberculosis be extensive, the great decrease in the healthy lung parenchyma may prove disastrous to the life of the patient. Consequently, the remedy is positively contra-indicated in widely-disseminated lung tuberculosis, unless a much smaller dose than I have yet heard of be employed. My idea is, then, that we may be able to reduce the dose, so that it will be neutralized before it stimulates inflammation throughout the entire tuberculous tissue, and in this manner the living tuberculous tissue may be acted on step by step, so as not to cut the life of the patient short by a general inflammation throughout the entire area of tubercular tissue at one and the same time. What I have said about extensive lung tuberculosis, I believe

will hold good regarding extensive tuberculosis of the larynx.

I cannot believe that a small cavity in the lung positively contra-indicates the use of the remedy. It is possible that the necrotic tissue will be absorbed and that the newly-formed walls in a number of cases will resist the attack of the living bacilli left in the necrosed tissue and cheesy masses.

In the treatment of mild cases of pulmonary tuberculosis, small doses of the liquid are used, the average initial dose being 0.001 c. c. About five or six hours after the injection there may or may not be a chill, followed by fever running from 102° F. to 106° F. The fever generally falls within two hours after it reaches its maximum, while sometimes it continues for forty-eight hours. The fever is not always in proportion to the size of the dose, so that at any time there may be an excessive rise after a prolonged period of moderate elevation. In one case the pulse increased to 160 and the respirations to 40. Diarrhœa is not an uncommon symptom. Enlargement of the spleen and the lymphatic glands is frequently perceptible. The patients often have an expression of great illness. The sputum frequently increases in quantity and contains necrosed tissue. The bacilli also increase in number after treatment, and you frequently find a change in the form of the bacilli resembling in morphology those we can cultivate on culture-media poor in peptones. After prolonged treatment both the sputum and bacilli decrease, while in many instances the tubercular process would seem to continue even after the injection of the liquid ceased to produce any reaction. The physical signs from percussion and palpation do not change except when an active inflammation is set up by the reagent, in what was not recognized as tubercle tissue.

To picture better the action of the remedy in pulmo-

nary tuberculosis, I will give you the following history of an interesting case in the Charité:

A girl, aged twenty-three years, who had been treated with morphine and creasote. Her father and mother died from phthisis, and she has sisters now suffering from the same disease. Menses began at the age of eighteen and have been regular.

She was healthy before the summer of 1888.

Nine weeks ago when she entered the hospital her muscles were flabby and she felt weak, but there was no loss of power.

Conjunctiva, lips, and oral mucous membrane anæmic. Tongue moist. Teeth good. Pulse normal. Form of chest good. Costal respiration somewhat increased on both sides. Lungs and heart of normal size. Slight dulness over left apex, but still some vesicular breathing, with a few crepitant râles. Dry, hacking cough.

Weight on entering, one hundred pounds. In three weeks she lost two pounds.

Bad cough, difficult expectoration, and slight pain in apices and other parts of the chest. Could not eat well. Cough caused vomiting. Night-sweats.

When she entered the hospital she could not sleep even after the administration of one-fourth of a grain of morphine.

November 19. Over right apex vesicular breathing. Dulness over left apex. Between the arytenoid cartilages there were to be seen projections forming the walls of ulceration.

21st. 0.002 c.c. of the Koch fluid injected. Slight nausea. Temperature rose to 38.3°. Expectoration increased. Pulse 100. Respirations 20.

22d. 0.005 c.c. of the Koch fluid injected. Morning temperature normal. At 6 P. M. 39.8° C. Pulse 124. Respirations 25. Spots on larynx slightly swollen. Cough looser.

23d. Morning temperature normal. Evening temper-

ature 37.6° C. Respiration 22, pulse 104. Gray spots appear on larynx.

24th. 0.005 c. c. injected. Morning temperature normal. At 6 P. M. 38.6° C. Slight friction-sound in left lung between axillary and mammary lines. Marked enlargement of the ulcers on the arytenoid cartilages. Left vocal cord shows grayish spots; moist râles in left apex. Increased dulness in left lung. Further enlargement of ulcers on arytenoid bodies. Bronchial breathing. Great weakness.

26th. 0.008 c. c. injected. Morning temperature normal. Evening temperature, 9 P. M., 40.1° C. Pulse and respiration unchanged. Cough increased. Expectoration lessened. Sleeplessness returned.

27th. No change.

28th. 0.010 c. c. injected. Afternoon temperature, 38.3° C.

29th. A markedly improved general condition. Area of dulness lessened. No râles to be heard excepting over right clavicle.

December 1. 0.013 c. c. injected. Afternoon temperature 38.8° C. Up to this time there was a gain in body-weight of two pounds.

4th. 0.015 c. c. injected. Afternoon temperature, 39.5° C. Pulse 130. Respirations unchanged. Area of dulness increased. An increase of râles. With these conditions, a general disturbance was manifest. Bacilli continue in as large numbers as at first.

8th. The patient has lost one pound.

This history is about an average one. It certainly teaches us very little excepting that if improvement in pulmonary phthisis occurs under the Koch treatment, it is exceedingly slow, yet at the same time it shows that there is little or no *immediate* danger in the use of the liquid in mild cases of pulmonary tuberculosis, unless in exceptional cases in which there happens to be tissue that is hypersensitive to the action of the remedy.

While watching the effects of the liquid on lupus, the question that arises is, After the treatment, what condition are the tissues in immediately adjoining those which were sufficiently tuberculous to necrose under the inflammatory process produced by the Koch fluid? Will this apparently healthy tissue in the human economy be rendered immune, or will it be rendered more susceptible to the tuberculous process?

Professor Koch personally informed me that he felt quite certain of the power of his remedy to cure lupus and very mild cases of laryngeal tuberculosis, but that he did not believe it safe at present to make any estimate of its therapeutic value in other forms of tuberculosis.

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